

pages 1485-1492), Davis et al. (New England Journal of Medicine, 1998, Vol. 339, pages 1493-1499), Poynard et al. (The Lancet, 1998, Vol. 352, pages 1436-1422) or Reichard et al. (The Lancet, 1998, Vol. 351, pages 83-87) in view of Abella et al. (Brit. J. Clin. Pharmacol., 1996, Vol. 42, pages 731-747) , and further in view of Sies et al.,(Am.J. Clin. Nutr., 1995, Vol. 62, pages 1315S-1321S).

Claims 7, 8 and 10-19 are directed to methods of treating a patient having chronic HCV infection with a therapeutically effective amount of a combination therapy of interferon-alfa and ribavirin to substantially lower HCV-RNA in association with a therapeutically effective amount of Vitamin E and Vitamin C to ameliorate ribavirin-related hemolysis. Thus, applicants' claimed invention, as amended, provides an improved HCV therapy by ameliorating the ribavirin-related hemolysis throughout the duration of the combination especially in the first 4 to 12 weeks, of therapy so as to produce a sustained virological response in more patients than previously possible.

McHutchinson et al., David et al., Poynard et al., and Reichard et al. each teach the use of interferon a-2b in combination with ribavirin to treat HCV. These four references fail to teach use of antioxidants much less the specific combination of the two antioxidants, Vitamin E and Vitamin C, to treat ribavirin-induced hemolysis. Only ribavirin dose reduction is taught.

None of the deficiencies of these four references are cured by Abella et al. which discloses the evaluation of the antioxidant activity of Vitamin E in the plasma of healthy volunteers to which an oxygen free radical initiator ("AAPH") was added. Nowhere in Abella et al. is there any teaching about treating HCV patients or ribavirin -induced anemia, much less any suggestion that the combination of Vitamin E with Vitamin C would be useful in treating ribavirin -induced hemolysis in HCV patients being treated with the ribavirin-interferon alfa combination therapy. Applicants assert that there is no motivation in Abella et al. alone or in combination with the above four references to make the modifications that are stated to be obvious.

None of the deficiencies of McHutchinson et al., David et al., Poynard et al., Reichard et al., and Abella et al. are cured by Sies et al. by Sies et al. discloses that antioxidants Vitamins E , Vitamin C, and beta-carotenoids react with free radicals to lower DNA damage, diminish lipid peroxidation and inhibit malignant transformation There is no teaching or suggestion in Sies et al. about treating HCV patients or ribavirin -induced anemia, much less any suggestion that the combination of Vitamin E with Vitamin C would be useful in treating ribavirin -induced hemolysis in HCV patients being treated with the

ribavirin-interferon alfa combination therapy. Applicants assert that there is no motivation in Sies et al., alone or in combination with the above five references to make the modifications that are stated to be obvious.

Applicants assert that there is no motivation in Sies et al., alone or in combination with Abella et al. to combine the two references to solve the problem in the other four references.

Applicants have discovered that ribavirin –induced hemolysis in HCV patients being treated with only Vitamin E and the ribavirin-interferon alfa combination therapy is **not significantly better** than ribavirin –induced hemolysis in HCV patients being treated with the ribavirin-interferon alfa combination therapy-in the absence of Vitamin E.

Applicants assert that there is no motivation in the references, alone or in combination to make the modifications needed to bridge the gap to the claimed invention. The combined teachings of the references do not suggest the claimed invention which specifies that a combination of two antioxidants in association with ribavirin and interferon-alfa be used to treat HCV. Only by hindsight reconstruction using applicants' claimed invention as a template can the gap from the prior art to the claimed invention be bridged.

Reconsideration and withdrawal of this ground of rejection are urged.

Claims 47-54 are rejected under 35 U.S.C. 103 as being unpatentable over McHutchison et al. (New England Journal of Medicine, 1998, vol. 339, pages 1485-1492), Davis et al. (New England Journal of Medicine, 1998, vol. 339, pages 1493-1499,), Poynard et al. (The Lancet, 1998, vol. 352, pages 1436-1422) or Reichard et al. (The Lancet, 1998, vol. 351, pages 83-87) in view of Abella et al. (Brit. J. Clin. Pharmacol., 1996, vol. 42, pages 731-747) of Sies et al.,(Am. J. Clin. Nutr., 1995, Vol. 62, pages 1315S-1321S) as applied to claims 7,8 and 10-19 above, and further in view of U.S. Patent 4917888 (Katre et al., 1990 ("the '888 patent").

The '888 patent discloses various pegylated proteins but cures none of the deficiencies in McHutchison, et al., Davis, et al., Poynard, et al., Reichard, et al., or Abella et al., alone or in combination.

None of these seven references, alone or in combination, teach use of the combination of Vitamin E with Vitamin C in association with the ribavirin-prgylated

interferon alfa combination therapy to treat HCV more effectively by ameliorating the ribavirin-induced hemolysis.

Reconsideration and withdrawal of this ground of rejection are urged.

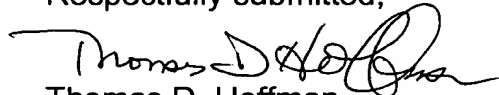
Claims 7,8,10-19, and 47-54 stand rejected under 35 U.S.C. 102(e) as being anticipated by Albrecht U.S. Patent No. 6,172,046 (Albrecht et al., 2001).

The Albrecht U.S. Patent teaches the use of interferon alfa or pegylated interferon alfa in combination with ribavirin to treat HCV. The Albrecht U.S. Patent fails to teach use of antioxidants much less the specific combination of the two antioxidants. Thus, the rejection of claims 7,8,10-19, and 47-54 under 35 U.S.C. §102(e) as being anticipated by the Albrecht U.S. Patent is not proper.

Reconsideration and withdrawal of this ground of rejection are urged.

Applicants assert that the claimed invention, as amended, is in statutory compliance with 35 U.S.C. § 103(a) and § 102(e).

Respectfully submitted,



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